Some questions for politicians

Reading party election manifestos (p 1754) and listening to political debates about health are depressing experiences. The politicians wax eloquent about their support for the National Health Service and their commitment to health education and preventive medicine but they have few practical proposals and usually duck behind parapets of generalities when asked specific questions.

Try asking politicians, for example, whether they support the continuing subsidy of butter (14·3p a pound) and milk by the European Economic Community at a time when medical advice is unanimous that people should be encouraged to eat less fat (and most medical experts support the substitution of margarine for butter).

Try asking politicians whether they would support proposals for Britain to follow the example of France and the United States and require all children attending state schools to be fully immunised against infectious disease. Those who retreat behind high sounding phrases about individual freedom of choice should be challenged about the continuing mortality and morbidity from preventable infections in Britain.

Try asking politicians who say they support the NHS how they propose that Britain should provide its citizens with access to the benefits of new technology in medicine—from coronary bypass surgery to joint replacement and kidney transplants—when the data show very clearly that fewer Britons receive these treatments than do Americans, Scandinavians, the French, and the Germans. Those doctors who may have reservations about more spending on high technology medicine may ask instead how soon Britain may expect to catch up with its European neighbours in providing adequate accommodation and care for the elderly.

And finally, try asking politicians what they propose to do about tobacco and alcohol, two proved causes of substantial ill health. Will they support a campaign to ban advertising, to boost health education, and to increase progressively the tax on these two health hazards as part of a strategy to reduce consumption?

These are not party political issues, so they provoke negligible concern among political journalists. They are matters of major concern to doctors. Let us make our voice heard on behalf of patients.

Regular Review

Luxuskonsumption, brown fat, and human obesity

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Some people who do not seem unduly afflicted by gluttony or sloth are very fat. Others, with a similar pattern of food intake and activity, are thin. This suggests that the thin people have some mechanism which burns off any excess of energy intake over normal requirements. The term "luxuskonsumption" was introduced to explain the observations of Neumann[1] and others that if a normal person increases his food intake above the requirements for maintaining his weight there is an initial increase in weight, but a new plateau is then established despite the continued overeating. Exactly what happens to the "missing" energy (that consumed in excess of baseline requirements, but apparently not stored as fat) has been a subject for controversy for the past 80 years. Recently *Clinical Science* has published a pair of invited reviews. One, by Hervey and Tobin, stated that observations supporting luxuskonsumption (or dietary induced thermogenesis, DIT, to use the current term) could be explained either by experimental error or by the known energy costs of the biochemical processes concerned in assimilating food.[2] The other, by Rothwell and Stock, stated that dietary induced thermogenesis existed, that it was an important factor in regulating body weight, and that the missing energy was burnt off in brown fat.[3] This review aims at showing where there is conflict, or common ground, between the two sides of the argument and at expressing a personal view about the relevance of these matters to human obesity.

Some observations are not in dispute. If a normal resting fasting subject is given a meal his metabolic rate will increase over the next hour and returns to baseline values within eight hours. This "thermic effect" is roughly proportional to the energy content of the meal, and for a mixed meal the extra energy expenditure is equivalent to about 8-10% of the energy content of the meal. The thermic response to a meal of protein is rather greater than that after an isoenergetic meal of carbohydrate or fat, but the old term "specific dynamic action" has been abandoned, since the thermic effect is also seen after protein free meals. It is technically difficult to measure the size of the thermic response to a meal for several reasons. Firstly, it requires very cooperative subjects to remain in the required state of relaxation for the eight hour observation period needed to regain baseline conditions. Secondly, the response is related to the baseline before the meal is given, and this baseline varies by about 5% from day to day in the same subject under standardised conditions. In a classic study 25 determinations of thermic response were made in 18 subjects, but some two fifths of the observations had to be discarded because the baseline differed by more than 2% from that obtained in other tests in the same subject.[4] Modern equipment for gas analysis has made

indirect calorimetry much simpler and more accurate, but the variation in baseline is still the principal factor limiting accuracy.

It is also generally agreed that normal people taking a diet with a low energy content show a decrease in resting metabolic rate[5 6] and that the same occurs with obese patients on a reducing diet.[7] Most workers also agree that the converse is true—that after a period of overfeeding the resting fasting metabolic rate increases.[8] Nevertheless, there is no consensus about the magnitude of this effect, its cause, or whether it differs between lean and obese people. This uncertainty is difficult to resolve in man because few volunteers are willing to be experimentally overfed by a sufficient amount to produce unequivocal results. Not only must the volunteers be willing to gain weight, they must also accept prolonged and rigid supervision of both energy intake and output, so that an energy balance sheet can be made which will withstand any criticism. The best study so far was that undertaken by the Vermont group on volunteers in the state prison, but unfortunately that study was designed to investigate the endocrine changes associated with experimental obesity in man, so that the energy balance data were not minutely documented.[9]

Researchers working with animals apparently have a great advantage, since they can impose any desired energy overload and study the effect on body composition by chemical analysis at the end of the experiment. By using large groups of genetically pure animals they have an enviable opportunity to escape the baseline fluctuation problem which plagues the clinical worker. Furthermore, if laboratory rats are allowed access to varied and palatable "cafeteria" food, rather than monotonous laboratory chow, they overeat and become obese,[10] but not as obese as they would have been expected to become if the excess energy had been stored as fat. Thus the cafeteria fed laboratory rodent seems to display the phenomenon of luxuskonsumption described by Neumann.[1]

The controversy in the *Clinical Science* reviews is mainly concerned with the interpretation of these animal studies.[2 3] I cannot analyse in full the arguments advanced by either side, but in essence Rothwell and Stock cite many publications in well refereed journals to show that cafeteria fed animals respond to overfeeding by increasing energy expenditure adaptively. Furthermore, this is achieved by thermogenesis in brown adipose tissue, which is also the main source of the extra heat generated in regulating the body temperature.[3] Hervey and Tobin say that diet induced thermogenesis does not exist as an adaptive response and hence does not need brown adipose tissue (or anything else) to carry this out.[2] They claim that the "missing" energy which is apparently eaten but not stored by cafeteria fed animals can be explained on two main grounds. Firstly, by errors in the measurement of energy intake and expenditure in the experiments cited by Rothwell and Stock, and, secondly, by the energy necessarily used in transforming excess dietary carbohydrate into stored fat. They cite experiments in which rats overfed by gavage laid down fat at a rate which would account for virtually all the excess energy intake, without leaving room for any luxuskonsumption.

Of the two sides in this dispute, Hervey and Tobin have the weaker position. Rothwell and Stock have not claimed that dietary thermogenesis can be induced by intragastric overfeeding, or even by cafeteria feeding in all strains of animals. Hence to disprove their findings it would be necessary to replicate their experiments—which Hervey and Tobin have not done. The calculation that Hervey and Tobin have used to account for all the excess energy is also suspect: the "estimated biochemical cost of synthesis," set at 20 kilojoules (4·8 kcal) for each 100 kilojoules of excess intake, assumes that dietary carbohydrate is being converted to stored fat, whereas a significant part of the stored fat must come from dietary fat, which can be deposited at much less metabolic cost. The figure of 20 kilojoules is derived from studies in which rats, pigs, and chickens[11–13] were overfed a mixed diet, so that it should include the cost of "digestion and absorption, approximately 8 KJ" which Hervey and Tobin use as an additional charge in their balance sheet.

The impartial critic must note that the arguments of the brown fat school also have weaknesses. If brown fat and dietary induced thermogenesis are important factors in regulating body weight, how is it possible to explain the wide variations between species, and even between strains of animals, in the activity of brown fat without corresponding differences in obesity?[3 14] When it is suggested that a defect in thermogenesis in brown fat is a cause of human obesity considerable faith is needed to sustain the argument.[15] James and his colleagues have compared the thermogenic response of obese subjects to a mixed meal[16] or infused noradrenaline[17] with that of thin subjects who "claimed to eat ad libitum." In each case the dosage of the thermogenic stimulus was calculated on the basis of ideal body weight, so the thin subjects (90·4% and 89·0% of ideal in the two experiments) received a bigger dose per kg than the obese ones. The thin subjects showed a greater response above baseline values to both stimuli, but in both cases their resting metabolic rate was so much lower than that of the obese ones that despite their "thermogenic defect" the obese subjects finished the experiment with the higher energy expenditure.

There is no evidence that obese adults with a strong family history of obesity, who might be expected to show the characteristics of a "thrifty gene," are characterised by a low resting metabolic rate[18] or a reduced thermogenic response to infused noradrenaline,[19] though there is a report that the young children of obese parents have a low energy expenditure.[20] The effect of several thermogenic stimuli on 24 hour energy expenditure of lean and obese women has been compared by direct calorimetry.[21] The obese women showed a slightly smaller thermogenic response than the lean ones to cool conditions, but by far the most striking difference between the two groups was the higher overall energy expenditure of the obese group. This study was conducted under conditions of negative energy balance for both lean and obese groups, so that the thermogenic capacity of the lean subjects may not have been fully displayed, but it is inconceivable that on a weight maintenance diet their thermogenic response would have been so large that they would have matched the obese group in energy expenditure overall.

It is not possible to conjure a unifying theory which will explain why some people become fat while others remain lean. This is too much to expect: economists have no simple explanation for the commercial success or failure of businesses or nations, and the energy economy of a human being is subject to as many complex influences as any financial economic model. We know that two people of the same age, sex, body composition, and pattern of activity may differ by 40% in energy expenditure,[22] so that differences in energy requirements do not necessarily lead to differences in energy balance. This implies that the control of energy intake is somehow accurately matched to requirements, but there is good evidence that this is often not so.[23] Stability in body weight is therefore a result of a balance between opposing forces, which may themselves change with time and different circumstances in any individual.

So, in the end, do we understand why some people eat far

more than others and there is so little apparent correlation between food intake and fatness? Has all this research advanced our ability to treat human obesity? The short answer to both questions is yes, although there are still topics of dispute on relatively minor points.

Energy expenditure, and hence energy requirements, is principally determined by the resting metabolic rate, which varies greatly among individuals.[24] The best single predictor of resting metabolic rate is lean body mass, but for people of similar lean body mass younger, heavier people have higher requirements than older, lighter people. The multiple correlation coefficient between age, sex, body composition, and metabolic rate is about 0·83,[25] so that 30% of the variation between individuals is unexplained by these factors. Genetic factors and measurement error probably contribute to this unexplained variability. An individual's resting metabolic rate can be influenced by overfeeding or underfeeding, and differences in physical activity and thermogenic responsiveness make further fine adjustments to energy expenditure.

Energy intake fluctuates widely within individuals from day to day,[26] but since the energy stores in normal man are equivalent to about 70 days' intake these fluctuations have little effect provided that the average intake over some weeks matches requirements. The sensations of hunger and satiety are very imprecise guides to energy requirements and are easily fooled by experimental manipulation.[27–29] Probably, like the laboratory rat, we would eat to match our requirements if we had access only to monotonous chow, but our physiological control systems cannot be expected to cope with the artifice of skilful cooks and food technologists. The last bastion of defence of normal body weight is cognitive control.[30] From the therapeutic viewpoint this is good news: it is always possible to find a diet on which an obese patient would, in time, achieve normal body composition. Nevertheless, the appropriate line of treatment varies with the patient, and in some cases the benefits of treatment would not justify the effort.[24]

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1 Neumann RO. Experimentelle Beiträge zur Lehre von dem täglichen Nahrungsbedarf des Menschen unter besonderer Berücksichtigung der notwendigen Eiweissmenge. *Arch Hyg (Berl)* 1902;**45**:1-87.

2 Hervey GR, Tobin G. Luxuskonsumption, diet-induced thermogenesis and brown fat: a critical review. *Clin Sci* 1983;**64**:7-18.

3 Rothwell NJ, Stock MJ. Luxuskonsumption, diet-induced thermogenesis and brown fat: the case in favour. *Clin Sci* 1983;**64**:19-23.

4 Strang JM, McClugage HB. The specific dynamic action of food in abnormal states of nutrition. *Am J Med Sci* 1931;**182**:49-81.

5 Benedict FG, Miles WR, Roth P, Smith M. *Human vitality and efficiency under prolonged restricted diet.* Washington DC: Carnegie Institution of Washington, 1919. (Publication 280.)

6 Keys A, Brozek J, Hanschel A, Mickelson O, Taylor HL. *The biology of human starvation.* Minneapolis: University of Minnesota Press, 1950.

7 Bray GA. Effect of caloric restriction on energy expenditure in obese patients. *Lancet* 1969;ii:397-8.

8 Garrow JS. The regulation of energy expenditure in man. In: Bray G, ed. *Recent advances in obesity research. 2.* London: Newman Publishing, 1978:200-10.

9 Sims EAH, Goldman RF, Gluck CM, Horton ES, Kelleher PC, Rowe DW. Experimental obesity in man. *Trans Assoc Am Physicians* 1968;**81**: 153-70.

10 Sclafani A, Springer D. Dietary obesity in adult rats: similarities to hypothalamic and human obesity syndromes. *Physiol Behav* 1976;**17**: 461-71.

11 Blaxter KL. Energy utilization and obesity in domesticated animals. In: Bray GA, ed. *Obesity in perspective.* Bethesda: National Institutes of Health, 1973. (DHEW Publication No (NIH) 75-708.)

12 Pullar JD, Webster AJF. The energy cost of fat and protein deposition in the rat. *Br J Nutr* 1977;**37**:355-63.

13 Van Es AJH. The energetics of fat deposition during growth. *Nutrition and Metabolism* 1977;**21**:88-104.

14 Brockway JM, Lobley GE. Thermogenesis in normal rabbits and rats: no role for brown adipose tissue? *J Physiol (Lond)* 1981;**314**:85-9.

15 Trayhurn P, James WPT. Thermogenesis—a control mechanism in obesity? 1. Brown fat may play an important role. *British Nutrition Foundation Bulletin* 1981;**6**:15-22.

16 Shetty PS, Jung RT, James WPT, Barrand MA, Callingham BA. Postprandial thermogenesis in obesity. *Clin Sci* 1981;**60**:519-25.

17 Jung RT, Shetty PS, James WPT, Barrand MA, Callingham BA. Reduced thermogenesis in obesity. *Nature* 1979;**279**:322-3.

18 Garrow JS, Blaza SE, Warwick PM, Ashwell MA. Predisposition to obesity. *Lancet* 1980;i:1103-4.

19 Danforth E Jr, Daniels RJ, Katzeff HL, Ravussin E, Garrow JS. Thermogenic responsiveness in Pima Indians. *Clinical Research* 1981;**29**:663A.

20 Griffiths M, Payne PR. Energy expenditure in small children of obese and non-obese parents. *Nature* 1976;**260**:698-700.

21 Blaza S, Garrow JS. Thermogenic response to temperature, exercise and food stimuli in lean and obese women, studied by 24 h direct calorimetry. *Br J Nutr* 1983;**49**:171-80.

22 Warwick PM, Toft R, Garrow JS. Individual variation in energy expenditure. *Int J Obes* 1978;**2**:396.

23 Porikos KP, Hesser MF, Van Itallie TB. Caloric regulation in normal-weight men maintained on a palatable diet of conventional foods. *Physiol Behav* 1982;**29**:293-300.

24 Garrow JS. *Treat obesity seriously: a clinical manual.* London: Churchill Livingstone, 1981.

25 Doré C, Hesp R, Wilkins D, Garrow JS. Prediction of energy requirements of obese patients after massive weight loss. *Human Nutrition: Clinical Nutrition* 1982;**36C**:41-8.

26 Acheson KJ, Campbell IT, Edholm OG, Miller DS, Stock MJ. The measurement of food and energy intake in man—an evaluation of some techniques. *Am J Clin Nutr* 1980;**33**:1147-54.

27 Pudel VE, Oetting M. Eating in the laboratory: behavioural aspects of the positive energy balance. *Int J Obes* 1977;**1**:369-86.

28 Wooley OW, Wooley SC, Dunham RB. Can calories be perceived, and do they affect hunger in obese and non-obese humans? *J Comp Physiol Psychol* 1972;**80**:250-8.

29 Booth DA. Satiety and appetite are conditions reactions. *Psychosom Med* 1977;**39**:76-81.

30 Garrow JS, Stalley S. Cognitive thresholds and human body weight. *Proc Nutr Soc* 1977;**36**:18A.